Curriculum Vitae

Date: May 2009

Name	First Name	Marital Status	Nationality
Manley	Paul	Divorced	U.K.
Date of birth	**Mother Language**	**Other Languages**	
25.12.1953	English	German	
Home Address		**Novartis internal address**	
Bruggweg 12 CH-4144 Arlesheim Switzerland		WKL-136.4.86 CH-4002 Basel Switzerland	
Email		**Pers.-No**	
paul.manley@novartis.com		5002315	

Professional Experience

Summary:

28 Years medicinal chemistry research experience in pharmaceutical industry (21 in Sandoz - Novartis), with extensive experience as a Program / Project Team Leader / Global Project Team Representative (Glivec & Tasigna). A proven track record for drug discovery in the Oncology, Respiratory, Cardiovascular and Anti-infective disease areas.

Key contributions to Oncology DA: Leadership of Novartis-SGX research collaboration. Recognising need for Glivec follow-up in 2000, rapid initiation of Bcr-Abl Program and discovery of AMN107 (nilotinib; ESC 2002, PoC 2004, NDA 2006) and championing development of drug to launch of Tasigna® in 2007 and beyond; building Jak2 program; initiation of Flt3 Program with identification of PKC412 as clinical candidate; development compounds for Angiogenesis Program.

Key contributions to Respiratory DA: Leadership of PDE4D Program with development compounds; deputy leadership of K-Channel Activator Program with Clinical Phase I compound (KCO 912).

Organisation of Scientific Meetings: Kinase Inhibitor sessions at European Med Chem Symposium (2006) and Medicinal Chemistry Session at 229th ACS (2005).

Organisation of Novartis Workshops: "Angiogenesis"; "Target & Lead Selection"; "Pharmacophore Modelling and Virtual Screening".

Faculty Member: Chronic myeloid leukaemia workshops, 2005, 6 & 7; Swiss Med. Chem. School, 2002 & 4; Novartis Med. Chem. Workshop, 2004.
Regularly Chair scientific meetings and reviewer of medicinal chemistry and oncology drug scientific publications.

Professional Experience

Career History:

1998 to date: NIBR Oncology: Principal Research Investigator; Novartis Leading Scientist.

Program Team Head: Leader of NIBR/SGX research collaboration (since 2006). Joint Leader of NIBR/GNF Bcr-Abl Program (2000-2006). Leader of JAK2 Program 2004-2005. Leader of Flt3 Program 2001-2002.

Global Project Team Research Representative: Tasigna (since 8/2004); Glivec (since 10/20080.

Chemistry Laboratory Head (1998 to date).

Scientific Chemistry Expert: Oncology Department (1999-2001).

Additional Responsibilities: Compound Champion AKU557/AMN107, AAL993. MMP-Program liason between Basel (Research and Pride) and Japan. Compound Profiling Team Head for PDE472A (1998-99). Workshops organised: "Angiogenesis"; "Target & Lead Selection"; "Pharmacophore Modeling and Virtual Screening".

RDTA Development Support: PCO912; PDE472.

Achievements: Design and synthesis of Bcr-Abl inhibitors: CSP(2007) **BQM647**; CSP(2005) **BGG463**; CSP(2004) **BBT594/LBY977**; ESC(2002) **AKU557/AMN107**). VEGF kinase inhibitors: ESC(2002) **AAX433/ABP309/AEB342**; ESC(2000) **AAL993**.

Novartis Leading Scientist award: 2007

ONC BU Presidents Prize 2004, 2006 and 2007: **AMN107 / Tasigna**.

1989-98: Sandoz / Novartis Respiratory Diseases

Program Team Head: Phosphodiesterase Inhibitors.

Chemistry Laboratory Head.

Additional Responsibilities: Steering Committee collaboration (Columbia University, NY): Utility of PDE inhibitors.

Achievements: Design and synthesis of PDE 4 Inhibitors (**FSC 229-472**; **ICC 222-520**). FSC declaration of **PDE472A**. Synthesis of NVP-AAD997-NX1 (thus confirming structure of PCO912 metabolite, M16). Design and synthesis of K_{ATP}-Activators (Phase I compound **EDP KCO 912, ICC 217-744**).

1986-9: Sandoz Cardiovascular

Chemistry Laboratory Head.

Achievements: Design and synthesis of K_{ATP}-Activators (**PCI 999**; design & synthesis of radioligand, marketed by Amersham).

1979-86 Searle Research & Development, High Wycombe, Bucks. HP12 4HL:

Group Leader (1981-86): Platelet & Vascular Dysfunction.

Research Investigator (1979-81): Antiinfectives.

Achievements: Design and synthesis of TxA_2 Synthase Inhibitors (Clinical Development Candidates), PDE 3 inhibitors, PAF antagonists, thrombin antagonists, Zenoconazole (orally-active antifungal). **Searle Merit Award (1986):** 'Discovery of two series of Thromboxane Synthase Inhibitors and two series of PAF-receptor antagonists'.

Education

Queen Elisabeth's Hospital School (1964-71)

Leicester University / Glaxo (1971-76): Applied chemistry; B.Sc. (Hons).

Liverpool University (1976-79): Organic chemistry; Ph.D.

G.D. Searle: C. Chem.; MRSC.

Unit Med. Chem., Oncology Basel **Function** Global Project Team Representative; Programme Team Head; Lab. Head: Sr. Research Investigator 2.		**Superior** Marc Lang
Promotions/Awards KTC **Novartis Presidents Award (2004):** AMN107 Early Development Team **Novartis Pharma Team (President's) Award honorary mention (2005):** AMN107 Development **Novartis Pharma Team (President's) Award (2007):** Tasigna Development **Novartis Leading Scientist Award (2007)**		**Special Tasks** IPT Representative (2004-) Programme/Project Team Head Chemistry Expert (1999-2001) Compound Champion Compound Profiling Team Head
Internal/External Courses/Sabbaticals **Courses:** **As faculty:** Novartis GDC Med. Chem. Workshop; Swiss Med. Chem. Course (2004; 2002); Nordwijkerhout Med Chem course (2005); Global Opinion Leader Summit CML 2006. **As delegate:** Vision to Practice, Risk Management, Negotiation Skills, Leading Teams **Sabbaticals:** None		

Publications

1. Paul W. Manley, Peter Drueckes, Gabriele Fendrich, Pascal Furet, Janis Liebetanz, Georg Martiny-Baron, Jürgen Mestan, Jörg Trappe, Markus Wartmann, Doriano Fabbro Extended kinase rofile and properties of the protein kinase inhibitor Nilotinib. *Biochim. Biphys. Acta* **2009**, *in press*.
2. P.W. Manley, S. Cowan-Jacob, D. Fabbro, G. Fendrich, W. Jahnke, J. Liebetanz, J. Mestan, A. Strauss, N. Vajpai, S. Grzesiek. Differences in the kinase binding modes of imatinib, nilotinib and dasatinib are reflected in Abl transphosphorylation assays. Acta Biochimica Polonica 2009;56:S4.
3. D. Fabbro, M. Warmuth, F.J. Adrian, P.W. Manley, S.W. Cowan-Jacob, G. Fendrich, A. Strauss, W. Jahnke, J. Liebetanz, J. Mestan, N. Vajpai, S. Grzesiek, J. Zhang, N. Gray. Acta Biochimica Polonica 2009;56:S5.
4. Eck, Michael J.; Manley, Paul W. The interplay of structural information and functional studies in kinase drug design: insights from BCR-Abl. Current Opin. Cell Biol. 2009:21:288-295.
5. Mahon F-X, Hayette S, Lagarde V, Belloc F, Turcq B, Nicolini F, Belanger C, Manley PW, Leroy C, Etienne G, Roche S, and Pasquet J-M. Evidence that Resistance to Nilotinib May Be Due to BCR-ABL, Pgp, or Src Kinase Overexpression. Cancer Res 2008;68:9809–16.
6. Cross, N. C. P.; Daley, G. Q.; Green, A. R.; Hughes, T. P.; Jamieson, C.; Manley, P.; Mughal, T.; Perrotti, D.; Radich, J.; Skoda, R.; Soverini, S.; Vainchenker, W.; Verstovsek, S.; Villeval, J.-L.; Goldman, J. M. BCR-ABL1-positive CML and BCR-ABL1-negative chronic myeloproliferative disorders: some common and contrasting features. Leukemia 2008;22:1975-1989.
7. Day E, Waters B, Spiegel K, Alnadaf T, Manley PW, Buchdunger E, Walker C, Jarai G. Inhibition of collagen induced discoidin domain receptor 1 and 2 activation by imatinib, nilotinib and dasatinib. Eur J Pharmacol 2008;599:44-53.
8. Dierks C, Beigi R, Guo G-R, Zirlik K, Stegert MR, Manley PW, Trussell C, Schmitt-Graeff A, Landwerlin K, Veelken H, Warmuth M. Expansion of Bcr-Abl-Positive Leukemic Stem Cells Is Dependent on Hedgehog Pathway Activation. Cancer Cell 2008;14:238.
9. Ganapathipillai, S.S.; Medova, M.; Aebersold, D.M.; Manley, P.W.; Berthou, S.; Streit, B.; Blank-Liss, W.; Greiner, R.H.; Rothen-Rutishauser, B.; Zimmer, Y. Coupling of Mutated Met Variants to DNA Repair via Abl and Rad51. Cancer Research 2008;68:5769-5777.
10. VajpaiN., Strauss A., Fendrich G., Cowan-Jacob S.W., Manley P.W., Grzesiek S., Jahnke W. Solution conformations and dynamics of ABL kinase inhibitor complexes determined by NMR substantiate the different binding modes of imatinib/nilotinib and dasatinib. J. Biol. Chem., 2008; 283:18292-18302.
11. Vajpai N., Strauss A., Fendrich G., Cowan-Jacob S.W., Manley P.W., Grzesiek S., Jahnke W. Backbone NMR resonance assignment of the Abelson kinase domain in complex with Imatinib. *Biomolecular NMR* Assign 2008;2:41-42.
12. Konig H, Holtz M, Modi H, Manley P, Holyoake T.L., Forman S.J., and Bhatia R. Enhanced BCR-ABL kinase inhibition does not result in increased inhibition of downstream signaling pathways or increased growth suppression in CML progenitors.

Leukemia 2008;22:748-755.

13. Gleixner KV, Mayerhofer M, Sonneck K, Gruze A, Samorapoompichit P, Baumgartner C, Lee FY, Aichberger KJ, Manley PW, Fabbro D, Pickl WF, Sillaber C, Valent P. Synergistic growth-inhibitory effects of two tyrosine kinase inhibitors, dasatinib and PKC412, on neoplastic mast cells expressing the D816V-mutated oncogenic variant of KIT. Haematologica 2007;92:1451-1459.

14. White DL, Saunders VA, Dang P, Engler J, Venables A, Zrim S, Zannettino A, Lynch K, Manley PW, and Hughes T. Most CML patients who have a suboptimal response to imatinib have low OCT-1 activity: higher doses of imatinib may overcome the negative impact of low OCT-1 activity. Blood 2007;110:4064-4072.

15. Shemon AN, Sluyter R, Stokes L, Manley PW, Wiley JS. Inhibition of the human P2X7 receptor by a novel protein tyrosine kinase antagonist. Biochemical and Biophysical Research Communications 2008;365:515-520.

16. Brownlow N, Russell AE, Saravanapavan H, Wiesmann M, Murray JM, Manley PW and Dibb NJ. Comparison of nilotinib and imatinib inhibition of FMS receptor signaling, macrophage production and osteoclastogenesis. Leukemia 2008;22:649-652.

17. White DL, Saunders VA, Dang P, Engler J, Venables A, Zrim S, Zannettino A, Lynch K, Manley PW, and Hughes T. Most CML patients who have a suboptimal response to imatinib have low OCT-1 Activity. Higher doses of imatinib may overcome the negative impact of low OCT-1 Activity. Blood First Edition Paper, prepublished online August 30, 2007;

18. Weisberg E, Manley PW, Cowan-Jacob SW, Hochhaus A, Griffin JD. Second generation inhibitors of BCR-ABL for the treatment of imatinib-resistant CML. Nature Rev. Cancer 2007;7:345-356.

19. White DL, Saunders VA, Lynch K, Manley PW, and Hughes TP. Imatinib increases the intracellular concentration of nilotinib which may explain the observed synergy between these drugs. Blood 2007;109:3609-3610.

20. Ray A, Cowan-Jacob SW, Manley PW, Mestan J, and Griffin JD. Identification of Bcr/Abl point mutations conferring resistance to the Abl kinase inhibitor AMN107 (Nilotinib) by a random mutagenesis study. Blood 2007;109:5011-5015.

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22. Cowan-Jacob, S.W.; Fendrich, G.; Floersheimer, A.; Furet, P.; Liebetanz, J.; Rummel, G.; Rheinberger, P.; Centeleghe, M.; Fabbro, D.; Manley, P.W. Structural biology contributions to the discovery of drugs to treat chronic myelogenous leukaemia. Acta Crystallographica, Section D: Biological Crystallography 2007;D63:80-93.

23. Manley PW, Cowan-Jacob SW, Fendrich G, Strauss A, Vapai N, Grzesiek S, Jahnke W. Bcr-Abl Binding Modes of Dasatinib, Imatinib and Nilotinib: An NMR Study. Blood 2006;108:224a.

24. Weisberg E, Catley L, Wright R, Andrew Kung1, Moreno D, Banerji L, Ray A, Manley PW, Mestan J, Fabbro D, Jiang J, Hall-Meyers E, Callahan L, Dellagatta JL, Kung A and Griffin JD. Beneficial Effects of Combining Nilotinib and Imatinib in Pre-Clinical Models of BCR/ABL+ Leukemias. Blood 2007;109:2112-2120.

25. Weisberg E, Wright R, Jiang J, Ray A, Moreno D, Manley P, Fabbro D, Hall-Meyers E,

Catley L, Podar K, Kung AL, Griffin JD. Effects of PKC412, nilotinib and imatinib against GIST-associated PDGFRA mutants conferring differential sensitivity to imatinib. Gastroenterology 2006; 131:1734-1742.

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33. Prenen H, Guetens G, de Boeck G, Debiec-Rychter M, Manley P, Schöffski P, van Oosterom AT, de Bruijn E. Cellular Uptake of the Tyrosine Kinase Inhibitors Imatinib and AMN107 in Gastrointestinal Stromal Tumor Cell Lines. Pharmacology 2006;77:11-16.

34. Adrian FJ, Ding Q, Sim T, Valenta A, Sloan S, Liu Y, Zhang G, Hur W, Ding S, Manley P, Mestan D, Fabbro D, Gray N. Allosteric inhibitors of Bcr-Abl dependent proliferation. Nature Chem. Biol. 2006;2:95-102.

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36. P.W. Manley, S.W. Cowan-Jacob, G. Fendrich, J. Mestan. Molecular Interactions Between the Highly Selective pan-Bcr-Abl Inhibitor, AMN107, and the Tyrosine Kinase Domain of Abl. *Blood* **2005**, 106, 940a-941a.

37. Fabbro, D., Fendrich, G., Guez, V., Meyer, T., Furet, P., Mestan, J., Griffin, J. D., Manley, P. W., & Cowan-Jacob, S. W. "Targeted therapy with imatinib: An exception or a

rule?", Handbook of Experimental Pharmacology (2005), vol.167, Inhibitors of Protein Kinases and Protein Phosphates, pp. 361-389.

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43. P.W. Manley, S. Cowan-Jacob, J. Mestan, Advances in the Structural Biology, Design and Clinical Development of Bcr-Abl Kinase Inhibitors for the Treatment of Chronic Myelogenous Leukemia. *Cell. Mol. Biol. Lett.* **2005**, 10, 62S-65S.
44. T.J. Boggon, Y. Li, P. Manley, M.J. Eck. Crystal structure of the Jak3 kinase domain in complex with staurosporine analogue AFN941. *Blood* **2005**, 106, 996-1002.
45. T. O'Hare, D.K. Walters, E.P. Stoffregen, T. Jia, P.W. Manley, J. Mestan, S. Cowan-Jacob, M.C. Heinrich, M.W.N. Deininger, B.J. Druker. In vitro activity of Bcr-Abl inhibitors AMN107 and BMS-354825 against clinically relevant imatinib-resistant Abl kinase domain mutants. *Cancer Res.* **2005**, 65, 4500-4505.
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47. E. Weisberg, P.W. Manley, W. Breitenstein, Josef Brüggen, S.W. Cowan-Jacob, A. Ray, B. Huntly, D Fabbro, G. Fendrich, E. Hall-Meyers, A.L. Kung, Jürgen Mestan, G.Q. Daley, L. Callahan, L. Catley, C. Cavazza, M. Azam, D. Neuberg, R.D. Wright, D.G. Gilliland and J.D. Griffin. AMN107: Characterization of a novel inhibitor of both wild-type and imatinib-resistant mutant Bcr-Abl in vitro and in murine models of leukemia. *Cancer Cell*, **2005**, *7*, 129-141.
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Presentations at Scientific Conferences

1. Design of BCR-Abl kinase inhibitors to treat imatinib-resistant leukaemia. International Symposium on Advances in Synthetic & Medicinal Chemistry Kiev, August 23-27, 2009.
2. Differences in the kinase binding modes of imatinib, nilotinib and dasatinib are reflected in Abl transphosphorylation assays. 6th International Conference: Inhibitors of Protein Kinases, Warsaw, 27 June – 1 July, 2009. ***Chairperson.***
3. Nilotinib: A step forward. 49TH Annual Scientific Meeting: British Society of Haematology, Brighton, 27 April, 2009.
4. Structure-based design & clinical efficacy of targeted anti-leukemic drugs: Imatinib, nilotinib & inhibitors of T315I mutant forms of Bcr-Abl. MEDI Lunch&Learn: Salt Lake City, ACS Meeting, 24 Mar 2009.
5. Structure-based design of nilotinib: A new therapy for resistant chronic myelogenous leukaemia (CML). 6th International Symposium for Chinese Medicinal Chemists (ISCMC). Shanghai, 28 July-1 August, 2008.
6. Nilotinib: From bench to bedside with a new therapy for chronic myelogenous leukaemia (CML). Meeting: Cellular Signaling & Molecular Medicine. Dubrovnik, Croatia, 29 May 2008.
7. The Future Perspective of Molecular Targeted Therapy based on the Experience of Imatinib Development. International Symposium on GIST Treatment. Osaka, 19 April 2008.
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9. Zielgerichtete Therapie der CML: Neue Option für die 2nd Line. Development of Nilotinib. Heidelberg; 1 February 2008.
10. Further TKIs for Haematological Malignancies. Second Global CML Workshop; Puerto Rico, 13 December, 2007.
11. Tasigna® (nilotinib): Discovery & profile of a new targeted BCR-ABL kinase inhibitor for CML. Targets & Targeted Drugs in CML: On the way to develop curative therapies, Vienna; 26-28 October, 2007.
12. Leukaemia Therapy: The discovery of imatinib & nilotinib. Swedish Läkemedelskongressen; Stockholm; 24 October, 2007.
13. Drug Discovery & Development for Treatment of Cancer: Tyrosine kinase inhibitors. Medical Oncology Group of Australasia 28th Annual Scientific Meeting; Melbourne, 3 August, 2007.
14. Discovery and development of the highly potent BCR-ABL specific TKI, Tasigna. Tasigna launch meeting; Berne; 14 June, 2007. ***Discussant on panel.***
15. Targeting BCR-ABL without the need for Multi-Targeted Kinase Inhibitors. 6th Annual Protein Kinase Congress; Lisbon; 22 May, 2007. ***Chairperson.***
16. Discovery of & Structural Biology Studies with Nilotinib, a Selective BCR-ABL Inhibitor for CML. Joint German-Swiss Medicinal Chemistry Meeting: "Frontiers in Medicinal Chemistry"; Berlin; 20 March, 2007
17. GNF2: A prototype allosteric inhibitor of ABL kinase. CML Workshop – Looking

Toward the Future; Bermuda; 15-16 Dec, 2006.

18. Bcr-Abl Binding Modes of Dasatinib, Imatinib and Nilotinib: An NMR Study. ASH, Orlando, FL, Dec. 9-12, 2006; #747: *Blood* 2006, 108(11 pt.1):224a.
19. Nilotinib: A new BCR-ABL inhibitor for the treatment of imatinib-resistant CML and GIST. "Targeting the Kinome" meeting, Basel, Switzerland, Dec 4-6, 2006.
20. Nilotinib: A new agent for the treatment of imatinib-resistant Chronic Myelogenous Leukaemia. Swiss Chemical Society, *"Herbstversammlung"*, Zurich, 13 October 2006.
21. New kinase inhibitors for the treatment of hematological malignancies and gastrointestinal stromal tumors. 232nd ACS National Meeting, San Francisco, CA, United States, Sept. 10-14, 2006; #MEDI-319.
22. Nilotinib: A Novel Bcr-Abl Kinase Inhibitor for the Treatment of Chronic Myelogenous Leukemia. Asia Pacific Education Center of Hematology / Oncology, Shanghai, 29 Aug, 2006.
23. Case Study: Gleevec - A New Treatment Modality for CML, Drug Discovery Technologies Europe, London, March 14-14, 2006.
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27. AMN107: A Novel Bcr-Abl Kinase Inhibitor for the Treatment of Chronic Myelogenous Leukemia. Pharm. Sci. Fair: Anti-Cancer Agents. Nice; June, 2005.
28. Case History: Imatinib. Cambridge, MA; June 2005. ***Faculty.***
29. Design and Synthesis of PDE472. Organic Synthesis and Process Chemistry. Hyderabad, 1-3 April, 2005
30. Structural biology guided optimization of tyrosine kinase inhibitors: AMN107 a selective and potent Bcr-Abl inhibitor. 229th ACS National Meeting, San Diego, CA, United States, March 13-17, 2005, MEDI-309. ***Chairperson/Session Organiser.***
31. Glivec: A case history. Swiss Course on Medicinal Chemistry. Leysin, Switzerland. October, 2004. ***Faculty.***
32. AMN107. Novartis Course on Medicinal Chemistry. Boston, MS. October, 2004. ***Faculty.***
33. Anthranilic Acid Derivatives: VEGF-R Kinase Inhibitors for Anti-angiogenic Therapy in Cancer. 18th International Symposium on Medicinal Chemistry, Copenhagen, August 2004.
34. Targeted drugs for cancer therapy: Glivec a new paradigm. 15th International Symposium on Molecular Biology of Haematopoiesis. Tokyo, August 2004.
35. Targeted drugs for cancer therapy. Gleevec: a new paradigm. Gesellschaft Deutscher Chemiker Aachen, June, 2004.
36. Targeted drugs for cancer therapy. Gleevec: a new paradigm. Freiburger Chemischen Gesellschaft, Feb., 2004.
37. Targeted drugs for cancer therapy. Gleevec: a new paradigm. New therapies for the treatment of cancer. North Eastern ACS Meeting, Cambridge, MS; December 2003.
38. A novel anthranilamide, as an anti-angiogenic VEGF receptor kinase inhibitor. Autumn Meeting of Swiss Chemical Society, Lausanne, 2003.

39. Glivec: A case history. 23RD Advanced Course on Medicinal Chemistry. Urbino, Italy. July, 2003. **Faculty.**
40. Advances with VEGF-R Kinase Inhibitors for the Treatment of Angiogenesis. 3rd International Conference on Inhibitors of Protein Kinases . Warsaw, June 2003. ***Chairperson.***
41. Targeted drugs for cancer therapy: A new paradigm. *CHEM 267.* Berkeley, CA. April, 2003.
42. STI571 (imatinib): A targeted drug for cancer. Biozentrum, Basel, January 2003.
43. PKC412 (Midostaurin): an Flt3 inhibitor with potential for the therapy of acute myelogenous leukemia. "Protein Phosphorylation". San Diego, March, 2003. *CHAIRPERSON.*
44. Targeted Cancer Medicine - a look into the future. European School of Oncology Winter-Masterclass: Clinical Oncology. Tenerife, 24 January, 2003.
45. Structural and enzymatic studies of interactions with Abl kinase and resistance mutants. "Protein Kinases in Drug Discovery & Development". San Francisco, October, 2002. *CHAIRPERSON.*
46. Molecular therapy of cancer – glivec and beyond. Taipei. September, 2002.
47. STI571 (imatinib): An inhibitor of Bcr-Abl activation. Granta Park Symposium. Cambridge. June 2002.
48. Glivec: A case history. Swiss Course on Medicinal Chemistry. Leysin, Switzerland. October, 2002.
49. Discovery of STI571 and preclinical studies. Tieteellinen juhlasymposium, Glivec: molekyylitasolta ihmisen elämään. Helsinki; March, 2002.
50. Molecular Design of Tyrosine Kinase Inhibitors. Second International Symposium on GIST- Tyrosine Kinase Inhibitors in Treatment of Solid Tumors. Helsinki, September, 2001.
51. Structure and Molecular Design of Tyrosine Kinase Inhibitors. Second International Symposium on GIST- Tyrosine Kinase Inhibitors in Treatment of Solid Tumors. Helsinki, September, 2001.
52. GLEEVEC (STI571): A tyrosine kinase inhibitor tailored for leukemia therapy. Gordon Conference on Medicinal Chemistry, New Hampshire, August, 2001.
53. Glivec and PTK787: Tailored kinase inhibitors for fitting cancer therapy. Society of Chemical Industry conference: "Protein Kinases: Good Targets of Drug Discovery", London, May 2001.
54. PTK787 / ZK222584. Discovery and Antiangiogenic Profile of a Selective VEGFR-2 Kinase Inhibitor. Gordon Conference on Medicinal Chemistry, New Hampshire, August, 2000.
55. Potassium Channel Activators for the Treatment of Asthma. and Disease. International Conference on ATP-Sensitive Potassium Channels and Disease, Illinois, July, 1998.
56. Potassium Channel Activators for the Treatment of Asthma: 6-Pyridylbenzopyran Derivatives. 214th ACS Meeting, Las Vegas, September, 1997.
57. PDE 4 Inhibitors: Design, synthesis and antiinflammatory activity of 4-(3-cyclopentylidenemethyl-4-methoxyphenyl)pyridine. Autumn Meeting of Swiss Chemical Society, Basel, 1996.
58. Structure-Activity Studies of Potassium Channel Opening in Pinacidil-Type Cyanoguanidines and Nitroethenediamines. Autumn Meeting of Swiss Chemical Society, Bern, 1991.

Posters at Scientific Conferences

1. Pierre Laneuville, Clifford DiLea, Jürgen Mestan, Ophelia Yin, Richard C. Woodman,

Paul W. Manley. Comparative In Vitro Cellular Data Alone is Insufficient To Predict Clinical Responses and Guide Choice of BCR-ABL Inhibitor To Treat Imatinib-Resistant Chronic Myeloid Leukemia (CML). *Blood* 2009;114(11 pt.1):#.

2. David A. Irvine, Bin Zhang, Elaine C. Allen, Tessa L. Holyoake, Marion Dorsch, Paul Manley, Ravi Bhatia, Mhairi Copland. The combination of Hedgehog pathway inhibitor LDE225 and nilotinib eliminates chronic myeloid leukemia stem and progenitor cells. *Blood* 2009;114(11 pt.1):#.
3. Pierre Laneuville, Clifford DiLea, Jürgen Mestan, Ophelia Yin, Paul W. Manley. Comparitive in vitro cellular data alone is insufficient to guide choice of BCR-Abl inhibitor to treat imatinib-resistant chronic myeloid leukemia (CML). European Society Haematology, Berlin, 6 June, 2009.
4. Paul W. Manley, Sandra Cowan-Jacob, Gabriele Fendrich, Janis Liebetanz, Jürgen Mestan, Nicole Martin, Doriano Fabbro. The inhibition of ABL kinase activity by nilotinib and imatinib, but not dasatinib, is time-dependent. *Proc. Am. Assoc. Cancer Res.* 2009;50:897.
5. Cullinane C, Natoli A, Hui Y, Conus N, Brueggen J, Manley PW, McArthur GA. Characterization of nilotinib activity against a model of KIT-induced neoplasia using FDG-PET. *Proc. Am. Assoc. Cancer Res.* 2008;49:561.
6. Davies A., Giannoudis A., Lucas C.M., Harris R.J., Manley P.W., Pirmohamed M., Clark R.E. Characterisation of nilotinib transport in CML cells. *Blood* 2007;118(11 pt.1):698a.
7. Extended kinase profiling of the BCR-ABL inhibitor nilotinib. Paul W. Manley, Josef Brüggen, Doriano Fabbro, Georg Martiny-Baron, Jürgen Mestan and Thomas Meyer. *Proc. Am. Assoc. Cancer Res.* 2007;48:772.
8. AMN107: Efficacy of the selective Bcr-Abl tyrosine kinase inhibitor in a murine model of chronic myelogenous leukemia. Michael Rugaard Jensen, Josef Brüggen, Clifford DiLea, Jürgen Mestan, Paul W. Manley. *Proc. Am. Assoc. Cancer Res.* 2006, 47:61-62.
9. Results with AMN107, a novel kinase inhibitor, in gastrointestinal stromal tumor (GIST): Preclinical rationale and early results in a patient (Pt) with imatinib (IM)-resistant GIST. P. Dileo, S. Bauer, A. Van den Abbeele, J. A. Morgan, S. George, J. M. Salesi, L. Veronese, P. Manley, J. A. Fletcher, G. D. Demetri. Gastrointestinal Cancers Symposium, San Francisco, 2006.
10. *In vivo* activity of AMN107, as selective Bcr-Abl kinase inhibitor, in murine leukemia models. J. Mestan, J. Brueggen, D. Fabbro, P. W. Manley, G. Gilliland, B. Huntly, E. Weisberg and J. D. Griffin. Journal of Clinical Oncology, 2005 ASCO Annual Meeting Proceedings. Vol 23, No 16S (June 1 Supplement), 2005: 6522.
11. Molecular Interactions Between the Highly Selective pan-Bcr-Abl Inhibitor, AMN107, and the Tyrosine Kinase Domain of Abl. Paul W. Manley, Sandra W. Cowan-Jacob, Gabriele Fendrich, Jürgen Mestan. *Blood* 2005, 106(11 pt.1):940a-941a.
12. AMN107: Efficacy as a selective inhibitor of the tyrosine kinase activity of Bcr-Abl in murine leukemia models. Paul W. Manley, Josef Brüggen, Sandra Cowan-Jacob, Doriano Fabbro, Gabriele Fendrich, Gary Gilliland, Brian Huntly, Andrew Kung, Jürgen Mestan, Ellen Weisberg, James D. Griffin. Blood 2004, 103(11 pt.1): Abst#.
13. AMN107: In vitro profile of a new inhibitor of the tyrosine kinase activity of Bcr-Abl. J. Mestan, E. Weisberg, S. Cowan-Jacob, D. Fabbro, P. Furet, G. Fendrich, G. Goutte, D. Kempf, M. Gaugler, J. D. Griffin, P. W. Manley. Blood 2004, 103(11 pt.1): Abst#.
14. Jürgen Mestan, Paul Manley, Thomas Meyer, Doriano Fabbro. An ELISA for PDGFR Phosphorylation: Comparison of effects of STI571 on Bcr-Abl, c-Kit and PDGFR-β

protein kinases. *PROC AM ASSOC CANCER RES* 2004, 45:Abs#1500.

15. Jürgen Mestan, Dominique Kempf, Gerard Goutte, Jonathan Fletcher, Paul Manley. A New ELISA for Cellular c-Kit Phosphorylation: Activity of STI571 Compared to that of other Protein Kinase Inhibitors. Blood 2003, 102(11 pt.2): Abs#4387.
16. Crystal structure of unphosphorylated c-Src in complex with an analogue of GleevecTM reveals relative orientations of the SH3, SH2 and kinase domains in the active conformation. Cowan-Jacob, Sandra W.; Fendrich, Gabriele; Liebetanz, Janis; Fabbro, Doriano; Manley, Paul W. Abstracts of Papers, 226th ACS National Meeting, New York, NY, United States, September 7-11, 2003.
17. Preclinical profile of PKC412 (midostaurin) as an FLT3 inhibitor for the treatment of AML. P.W. Manley, C. Boulton, G. Caravatti, J. Griffin, A. Kung, L. Kelly, M. Maira, J. Mestan, T. Meyer, S. Ruetz, E. Weisberg, D. Fabbro. *PROC AM ASSOC CANCER RES* 2003, 44:Abs 1004.
18. AAL993/ZK260255: A member of the novel anthranilic acid amide class of antiangiogenic VEGF receptor kinase inhibitors. Paul Manley, Guido Bold, Josef Brüggen, Pascal Furet, Jürgen Mestan, Thomas Meyer, Christian Schnell, Barbara Stolz, Jeanette Wood. *PROC AM ASSOC CANCER RES* 2003, 43:Abs 4697.
19. Molecular interactions between Gleevec and isoforms of the cAbl kinase. Paul Manley, Doriano Fabbro, Gabriele Fendrich, Pascal Furet, Sandra Jacob, Janice Liebetanz, Jürgen Mestan, Thomas Meyer. *PROC AM ASSOC CANCER RES* 2002, 43:Abs 4196. ***Selected for oral presentation.***
20. NVP-AAD777 / ZK202664, a selective VEGF receptor kinase inhibitor, which inhibits both VEGF- and bFGF-induced angiogenesis. *PROC AM ASSOC CANCER RES* 2001, 41:Abs 4470.
21. Structure-activity studies supporting a postulated binding mode of STI571 to Abl kinase. Abstr. Pap. - Am. Chem. Soc. (2001), 221st MEDI-143.
22. SAR Studies on the Angiogenesis inhibitor, PTK787 / ZK222584. 27th National Medicinal Chemistry Symposium, Kansas, June, 2000.
23. Rationalisation of the selective inhibition of VEGFR-tyrosine kinases by the angiogenesis inhibitor PTK 787 / ZK222584, on the basis of shape complementarity to hydrophobic domains within the ATP-binding site. AACR-NCI-EORTC Meeting on "Molecular Targets and Cancer Therapeutics", Washington, DC, November, 1999.
24. PDE 4 Inhibitors: Design, synthesis and antiinflammatory activity of 4-(3-cyclopentylidine-methyl-4-methoxyphenyl)pyridine. 212th ACS Meeting, San Diego, April, 1996.